CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
ACID BLUE 9

Chemical Code # 002154, Tolerance # 50315
SB 950 # 235
Original date: January 25, 2002, revised April 3, 2002

I. DATA GAP STATUS

Combined Chronic/Onco, rat:	Data gap, inadequate study, no adverse effect indicated
Chronic toxicity, dog:	Data gap, no study on file
Oncogenicity, mouse:	Data gap, no study on file
Reproduction, rat:	Data gap, inadequate study, no adverse effect indicated
Teratology, rat:	Data gap, inadequate study, no adverse effect indicated
Teratology, rabbit:	Data gap, inadequate study, no adverse effect indicated
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	Data gap, no study on file
DNA damage:	Data gap, no study on file
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.

All record numbers through 186058 in volume 020 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.

File name: T020403
Original: Kishiyama and Gee, 1/25/02, revised by Gee, 4/3/02.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED CHRONIC/ONCO, RAT

001 903933 Interim report summary for record no. 113562 below. "Long-Term Dietary Toxicity/Carcinogenicity Study in Rats (105 -week interim report)." (International Research and Development Corporation, December 19, 1979.) FD&C Blue # 1 was fed in the diet at concentrations of 0.1, 1.0, or 2% throughout a long term feeding study to 70 Charles River CD® rats/sex/group, beginning *in utero*. Summary reported no compound related effects other than blue coloration of hair, skin and feces. UNACCEPTABLE (insufficient information for assessment). (J. Remsen, 6/21/85).

50315 - 002 113562 Goldenthal, E. I. "Long-Term Dietary Toxicity/Carcinogenicity Study in Rats (105 -week interim report)." (International Research and Development Corporation, December 19, 1979.) FD&C Blue 1 was fed in the diet at concentrations of 0.1, 1.0, or 2% w/w throughout a long term feeding study to 70 Charles River CD® rats/sex/group, beginning *in utero* (F1 generation). Ten/sex/group were sacrificed at 12 months. The average consumption of FD&C Blue 1 was: males, 51, 520 or 1088 mg/kg/day; females, 63, 650 or 1336 mg/kg/day. Hair, skin, urine and fecal color changes were seen in all FD&C Blue 1 treatment groups. The report states that hair and skin color were normal after weeks 4 and 28, respectively, at 0.1%. Body weight was slightly reduced for the high-dose group. NOEL = 1% based on body weight and not determined, based on blue coloration. UNACCEPTABLE (missing tables and appendices, dose selection justification, analytical data). Possibly upgradeable. Adverse effects potential was not determined, due to lack of data. (Kishiyama and Gee, 1/22/02).

50315 - 002 113568 Mannell, W. A., H. C. Grice and M. G. Allmark "Chronic toxicity studies on food colours. V. Observations on the toxicity of brilliant blue FCF, Guinea green and benzyl violet 4B in rats." (Food and Drug Laboratories, Ottawa, Canada, published in *J. Pharm. & Pharmacol. 14: 378 - 384 (1962))* Brilliant blue (acid blue 9), purity not stated, was fed to 15 Wistar derived rats/sex at 0, 0.03, 0.3 or 3.0 % for 75 weeks, beginning at 30 to 37 days of age. There was no apparent affect on growth or food consumption. Most deaths, including controls, were due to respiratory disease and thought not to be treatment related. One male in each of the 0.3 and 3.0% groups died due to a tumor, location not identified. The summary table of histopathology did not clearly identify any target organ. UNACCEPTABLE (summary data only, too few animals per group, other deficiencies). No worksheet. (Gee, 1/22/02).

CHRONIC TOXICITY, DOG

No Study Submitted

ONCOGENICITY, MOUSE

No Study Submitted

REPRODUCTION, RAT

50315 - 002 113561 "A Three Generation Reproduction Study of FD&C Blue 1 in Rats". (Bio/dynamics Inc., Project No. 71R-738, October 19, 1973.) FD&C Blue 1 (lot CC1C-8, 92%) was admixed with the feed. Doses of 0, 10, 100, 300 or 1000 mg/kg/day were fed to Long-Evans rats for three generations. There were ten males and 20 females/group. Rats were fed FD&C 1 for two weeks before the mating of the F0 generation. The F0 generation were mated twice with the F1 selected from the F1b litters. The F1 adults were mated three times with half of the females (10) being sacrificed on day 19 for fetal evaluation. The remaining litters contributed pups for necropsy at weaning. The F2 adults were mated once with the offspring (F3a), being necropsied. Five/sex from the controls and high dose groups from the F1 parents and F3a offspring were examined histopathologically. Reduced bodyweights for F_1 and F_2 generation high-dose offspring were reported. Parental NOEL and pup NOEL could not be determined, due to lack of data. UNACCEPTABLE (all data were missing, including tables and appendices; no analyses of diets for test article; inadequate number of animals for histopathology). Probably not upgradeable. (Kishiyama and Gee, 1/18/02)

001 903931 Summary of 002 113561.

TERATOLOGY, RAT

001 903928 Summary of 002 113559. (J. Remsen, 6/21/85 and Gee, 1/18/02).

50315 - 002 113559 J. A. Kasner [Smith, J. M., Director of Toxicology] "Segment II Rat Teratology Study" (Bio/dynamics Inc., Project No. 71R-719C, 1971.) FD&C Blue #1 (92%) was administered via intubation at doses of 0, 200, 600 or 2000 mg/kg/day to 22-24 mated Long-Evans female rats/group, during days 6 through 15 of gestation. There were no effects on weight gain, pregnancy, live fetal litter size, resorptions, fetal weight, sex ratios, malformations or ossification variations by fetal counts. Because all of the appendices with individual data were missing, an independent evaluation by litter was not possible. Trypan blue, 30 mg/kg, positive control, did result in lower weight gain, an increase in the total number of malformed fetuses and a significant increase in the mean number of resorptions. Maternal and Developmental NOEL = 2000 mg/kg/day. UNACCEPTABLE (all appendices of individual data were missing, the three control groups need clarification, no analysis of dosing solutions). Possibly upgradeable. (Kishiyama and Gee, 1/18/02).

TERATOLOGY, RABBIT

50315 - 002 113564 Murchio, A **"**Segment II Rabbit Teratology Study". (Bio/dynamics Inc., Project No. 71R-721C, no date) FD & C Blue #1 (batch CCIC-8, 92%) was administered via gavage at doses of 0 (0.5% methylcellulose), 20, 60 and 200 mg/kg/day to 15-19 mated sexually mature female New Zealand rabbits/group during gestation days 6 through 18. Thalidomide was used as a positive

control. There were no statistically significant findings in any group treated with FD&C Blue #1 in either the does or the fetuses. Thalidomide was effective. Maternal and Developmental NOEL = 200 mg/kg/day. UNACCEPTABLE (missing appendices of data, no analysis of dosing materials, no dose justification). No adverse effect identified in the study as conducted. Possibly upgradeable with submission of missing information. (Kishiyama and Gee, 1/22/02).

001 903927: Summary of 113564. **"**Segment II Rabbit Teratology Study". Bio/dynamics Inc., Project No. 71R-721C. UNACCEPTABLE (insufficient information for assessment). (J. Remsen, 6/21/85).

GENE MUTATION

** 50315 - 008, 020 174635, 186058 Paika, I. J. "*Salmonella Typhimurum* Reverse Mutation Assay". (Toxikon Corporation, Project Number 92G-0513, April 24, 1992.) Lake Colorant II (EXP1056, purity not stated) was tested at concentrations of 0, 0.1, 1, 10, 100, 1000 and 10000 µg/plate for the potential to induce histidine reversion in *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537. There were triplicate plates in a single trial. The test article was slightly toxic at 10000 ug/plate in all strains. The number of revertants did not increase with Lake Colorant II exposure. UNACCEPTABLE (test article description and purity, concentrations of positive control compounds). Reviewed as upgradeable. (Kishiyama and Gee, 1/22/02).
Record no. 186058 in 50315-020 contained additional information regarding the test material used, although the data were from 1997. The test article contained 64% acid blue 9. Accompanying the volume was a letter from Toxikon, dated 2/12/02, giving the concentrations of the positive controls. With this additional information, the study has been upgraded to acceptable status with minor deficiencies. No additional worksheet. (Gee, 4/3/02)

CHROMOSOME EFFECTS

No Study Submitted

DNA DAMAGE

No Study Submitted

OTHER STUDIES

50315 - 002 113567 Hess, S. M. and Fitzhugh, O. G. "Absorption and excretion of certain triphenylmethane colors in rats and dogs." (FDA, published in *J. Pharmacol. Exp. Ther.* 114: 38-42 (1955)). A dose of 200 mg FD&C Blue No. 1 was given orally as a 2% solution in water to 3 rats/sex and the fecal excretion determined as 96% of the dose. Bile excretion was measured in 2 canulated dogs, given 200 mg in capsules, as 2.3 and 0.7% of the dose. No color was found in the urine. The

conclusion of the authors was that almost all of the material was excreted in the feces. No worksheet. (Gee, 1/22/02).